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13. ABSTRACT *(Maximum 200 words)*
This case-control study explores associations between breast cancer in San Francisco Bay Area women and body burdens of organochlorine chemicals, including dioxins, furans, PCBs and pesticides. The selected chemicals are lipophilic, they bioaccumulate, and have carcinogenic, estrogenic or anti-estrogenic properties. Cases (n=50) are women with malignant disease and controls (n=47) are women with benign histologic changes. Small samples of breast adipose were obtained during surgery and participants were interviewed on suspected risk factors. Preliminary results showed low to moderate levels for most chemicals, comparable to levels found in general population studies. A wide range of lipid content was observed, mandating expression of results on a lipid basis. Preliminary analysis suggests that age-adjusted ORs do not differ statistically from 1 for the dioxin and furan congeners examined. Cases and controls were similar in all covariates examined, reducing the likelihood of confounding by other potential risk factors. More analyses are underway to examine ORs for PCBs and pesticides; correlations among all chemicals; variables predicting elevated body burdens; and to further refine these preliminary results. A small but statistically significant decrease in average dioxin body burdens was observed when the study controls were compared with adipose samples collected from the San Francisco Bay Area in the late 1980s.

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INTRODUCTION

In this study. we took an innovative approach to addressing a significant data gap in the currently controversial hypothesis of environmental links to breast cancer. The design required an interdisciplinary, multi-institutional team of investigators using state-of-the-art tools of clinical practice, epidemiology and laboratory science. Our team is currently conducting two studies in the San Francisco Bay Area examining associations between breast cancer and the presence of certain chemicals in women undergoing breast surgery. The chemicals we are studying (dioxins and furans, individual PCB congeners, organochlorine pesticides) were chosen based on their carcinogenic, estrogenic or antiestrogenic activities. The first study, funded by this DOD grant, recruited women of all races from Stanford University Hospital, while the second study targets African American women from Kaiser Hospital in Oakland. This Final Report summarizes our findings from the first study. We expect to combine these data with data from the second study to enhance our statistical power.

BACKGROUND

In the US, breast cancer is the most common cancer in women and the leading cause of death in women between the ages of 40 and 55 [1]. All known risk factors, however, are estimated to account for fewer than 30% of breast cancer cases [2]. In the US, incidence rates have increased at a rate of 1.6% per year between 1973 to 1995 [3]. Although this increase is thought to be mainly due to earlier detection as a result of enhanced screening [4], part of the increase may be due to environmental factors. Extensive use of organochlorine pesticides and industrial chemicals in the first decades after WWII and the bioconcentration potential of these compounds in the food chain and in human tissues [5] may have placed a cohort of men and women at a high risk of exposure. As these women approach menopausal age, a well-documented risk factor [6], their body burden of these chemicals may place them at an even higher risk for developing breast cancer. A number of recent studies [7-18] have explored links between breast cancer and the presence of certain of these chemicals in human tissues. These studies vary in terms of sample size, matrix analyzed (serum vs. adipose), selection criteria and confounder adjustments. In the more recent and better designed studies, positive associations were found for β-HCH [9], DDE [10,11,12], DDT [10], PCB[10,18] and OCDD[15]. On the other hand, no associations were found for DDE [13,14,16], or β-HCH [12] in subsequent studies. The inconsistency in these findings is noteworthy; DDE was the only chemical positively identified in more than one study. We believe that, in addition to differences in the design of the above studies (selection of cases and controls, covariates, statistical power), the selection of chemicals for analysis may have contributed to the inconsistent and conflicting results. A careful selection of chemical compounds which may be associated with the development of breast cancer is essential in the design of a study focusing on environmental risk factors.

The critical role of sex hormones in the development of breast cancer is well-accepted [19-21]. Experimental evidence indicates two mutually exclusive pathways in the metabolism of estradiol. One pathway leads to the formation of 2-hydroxyestrone (2-OH-E), a non-genotoxic metabolite with minimal estrogenic activity. The second pathway leads to the formation of 16-alpha hydroxyestrone (16a-OH-E) a genotoxic metabolite with high estrogenic activity [22]. It has been proposed that exogenous compounds may activate or inhibit each of these pathways [23]. Increases in the ratio of 16a-OH-E to 2-OH-E have been linked to breast cancer, while decreases appear protective. As an example, indole-3-carbinol, an ingredient of cruciferous vegetables decreases this ratio and also decreases the incidence of mammary tumors [24]. On the other hand, a number of chlorinated organic compounds, PAHs and pharmaceuticals are thought to increase the ratio of 16a-OH-E to 2-OH-E [23], or even act as direct estrogens. The direct estrogenic potential of some of the DDT analogs is well-documented [25-27]. There is also experimental evidence on the estrogenic properties of other chlorinated pesticides such as Methoxychlor [27], Beta-HCH [28], Heptachlor [29], Chlordane [29] and Kepone [29-31]. It would be desirable, therefore, to include such

chemicals, as well as their metabolites (e.g., oxychlordane, heptachlor epoxide, etc.) and chemicals with similar structure (e.g. Mirex as a structural analog of Kepone) in a study of xenobiotics and breast cancer.

It is well known[32] that specific congeners of Polychlorinated Dibenzo-p-Dioxins and Polychlorinated Dibenzofurans (PCDD/PCDFs) and Polychlorinated Biphenyls (PCBs) have significantly different potency in inducing diverse enzymes, modulating hormone receptor-binding activities, altering levels of thyroid hormone and vitamin A, and resulting in immunotoxicity, teratogenicity, hepatotoxicity, cancer and acute toxicity in various cell systems and animals. Of the over two hundred dioxin and furan congeners, seventeen are chlorinated in the 2,3,7,8 positions. The most extensively studied congener of this group is 2,3,7,8 tetra dioxin (TCDD). All seventeen congeners have a planar structure, exhibit the highest affinity for the Ah receptor [32] and bioaccumulate in human tissues [33]. Of the 209 Polychlorinated Biphenyls (PCBs), those substituted on both para- and at least two meta- positions are approximate isostereomers of 2,3,7,8 TCDD and exhibit high affinity for the Ah receptor [32]. Additionally, mono-ortho coplanar congeners exhibit affinity for the Ah receptor, but at a lower level. Recently, the anti-estrogenic potential of a number of these PCDD/PCDF and PCB congeners has been shown [34-37]. In general, their order of potency paralleled their binding affinities for the Ah receptor [34]. Unless these specific congeners are measured and controlled for in the analysis, exposures may be misclassified and associations missed.

APPROACH

We decided to examine the value of analysing breast adipose tissue for a wide range of chemical compounds that have the following properties:

- They are lipophilic with long half-lives in human adipose tissue resulting in bioaccumulation, and
- There is evidence for their carcinogenicity and/or their estrogenic or anti-estrogenic potential.

HYPOTHESIS/PURPOSE

The purpose of the study is to drastically expand and refine the panel of chemical compounds that have been suspected of an association with breast cancer. Target compounds include PCDDs/PCDFs; specific congeners of PCBs (rather than total PCBs); and chlorinated pesticides with demonstrated carcinogenic or estrogenic/anti-estrogenic potency.

The hypothesis to be tested can be formulated as follows:

Ho: For each chemical compound targeted, there is no statistically significant difference in its concentration in breast adipose tissue of cases and controls.

TECHNICAL OBJECTIVES

The aim of the study is to elucidate the associations between breast cancer and the presence of organochlorine pesticides and specific PCB and PCDD/PCDF congeners in adipose tissue of women undergoing breast surgery.

The specific objectives of the study are:

1. To recruit, screen and select women for participation in the study.
2. To administer a questionnaire on medical and reproductive history, dietary habits and other health behaviors, environmental exposures, demographics and socioeconomic status.
3. To obtain samples of breast adipose tissue during surgery.
4. To analyze the adipose samples for a panel of chemicals.
5. To determine any correlations between chemicals measured in tissues of cases and controls. This would allow us to a) control for highly correlated measurements in a multivariate analysis of the data,

and b) identify chemicals which can be used as surrogates for others, therefore reducing the number of analytes that would need to be measured in future studies.

6. To use multivariate logistic regression to calculate exposure-specific odds ratios while controlling for other risk factors, including other chemical compounds.

METHODS

STUDY POPULATION

The study subjects were recruited from among women undergoing open surgical biopsy, lumpectomy, or mastectomy at Stanford University Hospital. Stanford is a referral hospital drawing patients from a wide area in Northern California. Because of low recruiting rate, we expanded the study to another area hospital, Kaiser-Oakland. Ten patients (3 cases and 7 controls) were recruited through Kaiser. While the study population is not representative of the general population of the State, it is representative of women at highest risk for breast cancer: predominately white and of higher socioeconomic status. The demographic and clinical profiles of study subjects are compared to those for Stanford Hospital in general and, for breast cancer cases, to those reported via the population-based surveillance system covering the greater San Francisco Bay Area.

For the purpose of this study, cases are defined as women with definitive breast malignancies, and controls as women classified with benign histologic changes. Because of the strong association between atypical hyperplasia and subsequent breast cancer, women with atypical hyperplasia are excluded from the control group. Women with carcinoma in situ are also excluded as this is thought to be a tumor marker for elevated risk for development of future breast cancer in either breast. Also excluded from both the case and control groups are women with previous cancer diagnoses and women taking tamoxifen. Controls are frequency matched to cases on age. A total of 50 cases and 50 controls was targeted for the study.

QUESTIONNAIRES

All study-eligible women were asked to sign a consent form and a medical release for access to medical records information, including the pathology report and associated diagnostic data. The participants were interviewed with two questionnaires:

1. Dietary Questionnaire. The dietary instrument is Gladys Block's short (60-item) inventory. The instrument has been used in a variety of cancer epidemiology studies by the California Department of Health Services, and serves well to estimate relative consumption of many dietary constituents, including total percent calories from fat.
2. Breast Cancer Study Questionnaire. The in-person interview solicits information on medical and reproductive history, family history, occupational and environmental exposures, health habits, and demographic characteristics.

Both the Dietary and the Breast Cancer questionnaires have the patient's medical record number as the sole identifier to ensure confidentiality during data review and coding.

SAMPLE HANDLING

In women undergoing surgical breast biopsy or wide local excision (lumpectomy or tylectomy), about 2 grams of breast adipose tissue were obtained from beyond the edges of the biopsy or excision cavity. For women undergoing mastectomy, similar amounts of breast adipose tissue were obtained from a site distant from the tumor in order not to interfere with pathologic analysis. The removed adipose tissue was immediately placed in chemically clean glass jars with teflon-lined screw caps. The jars were labeled with the medical record of the patient, with no other identifiers to ensure confidentiality and unbiased

chemical analysis. Samples were frozen to below -20 C° and transported to the Hazardous Materials Laboratory (HML) for analysis.

HISTOPATHOLOGY

Histologic sections of all breast lesions were evaluated by the Stanford University Department of Pathology. Diagnoses were coded as invasive malignant disease, non-invasive malignant disease, or benign histologic changes. Patients with breast disease classified as atypical hyperplasia or carcinoma in situ were excluded from the analysis.

DATA TRACKING

All completed questionnaires, medical records and pathology reports were kept by the PI in a secure filing cabinet. Questionnaire information was extracted, coded and entered in a computerized data base specifically designed for the study (FilemakerPro). The patient's medical record number was the sole identifier in this data base. Chemical analysis results were compiled in EXCEL spreadsheets. Questionnaire data and chemical analysis data were merged and subjected to statistical analysis using SAS.

PRELIMINARY RESULTS & DISCUSSION

POPULATION CHARACTERISTICS

Since the study design called for 50 cases and 50 controls frequency matched on age, we recruited, collected specimens from, and interviewed over 170 patients to form an eligible pool. Patients were excluded based on the pathology report (DCIS, or atypical hyperplasia); language difficulties; or prior cancer revealed during the interview. Because of slow recruiting rates, we added a second site, Kaiser-Permanente Hospital in Oakland. A total of 10 Kaiser patients (3 cases and 7 controls) were included in the study. At the end of the study there were 99 eligible participants with completed questionnaires and chemical analyses. Of the samples analyzed, two could not be used because they contained extremely low lipids and the target analyte concentrations were mostly below detection. There were, therefore, 97 eligible participants with analytical results (50 cases and 47 controls).

Using incidence data from the California Cancer Registry, we compared the age and race/ethnicity of the breast cancer cases in this study to all cases of invasive breast cancer treated at Stanford Hospital in 1995 (the most recent year with complete data) (Table 1). Cases in our study and at Stanford are predominantly Non-Hispanic White. Our study population, however, is dominated by subjects in their 40s (48%) while at Stanford most of the breast cancer patients are age 60 and older (42%). This skewed age-distribution is a result of our efforts to balance the age frequencies between the cases and controls which favored women in their 40s, the age range with the most overlap. Because this age distribution does not reflect the distribution of the majority of women with breast cancer, such differences must be taken into account when extrapolating findings of this study. On the other hand, our study population has a high proportion of premenopausal women, allowing for future sub-group analyses. A review of hospital accession data will allow us to further examine how representative our study population is of the population served by the hospital, and of the San Francisco Bay Area population at large.

Extensive covariate information was collected from cases and controls via in-person interview and self-administered dietary questionnaire. These study instruments were designed to collect information on traditional risk factors (e.g., family history, age at menarche, age of first full time pregnancy, parity, radiation exposure), equivocal risk factors (e.g., alcohol, dietary fat, physical activity, BMI), and more speculative risk factors (e.g., pesticide exposures, EMFs, occupational exposures). The distribution of selected covariates for the 97 participants (50 cases and 47 controls) are shown in Tables 2a-k. For most covariates, Pearson chi-square statistics and p-values were used to compare the distributions between

cases and controls. The Mantel Haenszel chi-square, which tests whether there is a linear association between the covariates and disease status, was used to compare the distributions of ordinal covariates.

Despite our efforts to frequency match by age, cases remained slightly older than controls ($p = 0.09$). Otherwise, cases and controls were remarkably similar. Overall, cases and controls did not differ in their reported sociodemographic characteristics, radiation exposures, medical histories, family histories, hormonal exposures, exercise habits, or exposures to occupational, environmental and household toxic substances. Most importantly, they did not significantly differ in any of the reported reproductive characteristics, several of which are considered to be among the strongest risk factors for breast cancer (e.g., early age at menarche, late age at first live birth). It is possible that the comparison of some of these covariates may have been confounded by the age difference between cases and controls. Future analyses will explore the relationship between some of these covariates and age.

DIET QUESTIONNAIRE INFORMATION

Information on dietary habits were extracted from the Block Food Frequency and Health Habits Questionnaire. A preliminary analysis of selected dietary covariates is presented in Table 2k. Subjects who reported daily caloric intakes of less than 600 kilocalories were considered unreliable and therefore excluded from the analysis (n=3). From this analysis, no case-control differences were observed for total caloric intake, percent calories from fat, fruit and vegetable consumption, dairy product consumption, meat consumption, egg consumption, smoking, or alcohol intake.

HISTOPATHOLOGY

Histopathology information was obtained from the Pathology Department of the participating hospitals. A copy of the pathology report was reviewed for the definitive diagnosis and, for the cancer cases, additional tumor information was extracted including TNM staging; cell type; tumor size; histologic grading determined by nuclear atypia, mitotic activity, and tubule formation; and angiolymphatic perineural invasion. For invasive tumors only, presence of axillary lymph node metastases; estrogen and progesterone receptor status (ER, PR). Of the 50 cases, 37 (74%) were classified as ER(+). An analysis of just the ER(+) cases is planned in the near future.

We observed a high proportion of women with Carcinoma In Situ, paricularly DCIS, recruited into our study. Since these women could not be included in either the Cases or the Control groups, their specimens were archived in search of additional funding that would allow analysis of these women as a separate exposure group. Inclusion of this third group would enhance our power to establish dose-response relationships for variables showing significant differences in cases and controls.

LIPID CONTENT

An important finding of the study was the high variability in lipid content observed in the adipose specimens. Lipid content ranged from less than 10% to over 90% with a mean of 72%. This variability may be explained by breast tissue physiology, where adipose is interspersed within non-fatty connective tissue. It may also reflect differential presence of blood or other non-lipid tissues in the sample submitted for analysis. Given the small size of these samples (often less than 1 g), these non-fatty tissues may impact the lipid content. To compensate for these differences, all results were expressed on a lipid basis, making all measurements comparable. As shown in Figure 1, the % lipid content of the adipose specimens correlated with the age of the patient ($R^2=0.12$, $p<0.001$). Given that age is a known risk factor for breast cancer, non lipid-adjusted concentrations may lead to misclassifications and significantly confound Odds Ratios for disease. It should be noted that some of the studies examining links between organochlorines and breast cancer did not use lipid adjusted measurements, which may explain, in part, the contradictory findings of those studies. Table 3 shows all these studies, the type of sample used

(adipose, serum, plasma), the analytes (if any) that were associated with breast cancer, and the type of lipid adjustment performed (gravimetric, enzymatic, or none).

CHEMICAL ANALYSES

Measurements of the major analytes are summarized in Tables 4 and 5 and in Figures 2, 3, 4 and 5. All PCDD/PCDF analyses have been completed and are presented in this Report. The percentage of samples that were measured above the respective detection limit for each analyte is also shown in Tables 4 and 5. More "non-detects" were observed in the controls than in the cases, reflecting overall lower levels in the controls. PCDD/PCDF measurements are used in a preliminary case-control analysis and PCDD/PCDF body burdens measured in the controls only are compared to other appropriate populations. This is the first time that PCDD/PCDFs were systematically measured in a California population.

Major dioxin and furan congeners are shown in Fig.2 for cases, controls, and a comparison population. The pattern of these congeners is consistent with patterns observed in other non-occupationally or non-accidentally exposed populations[38-39]. Specifically, the higher chlorinated dioxin congeners (OCDD, HpCDD and 123678HxCDD) are found at higher levels than the lower chlorinated (TCDD, PeCDD). Among the furans, 23478PeCDF is the most prominent. Dioxin and furan measurements in breast adipose tissue samples collected in our study are compared to unpublished dioxin and furan measurements in adipose tissue from 17 women collected in 1988[40]. These data originated from San Francisco Bay Area women undergoing surgery in 1988 for reasons other than cancer and they, therefore, constitute an appropriate comparison group to our study's controls. Because of the small size of our tissue samples (sometimes less than 0.5 g), some PCDD/PCDF congeners were below detection ("non-detect"). In such cases, half the detection limit was used fir the particular congener concentration. In addition, I-TEQs, the summary measures of PCDD/PCDF toxicity, were calculated using half the detection limit of the non-detected congeners, possibly inflating the I-TEQ. To facilitate comparisons with the other data set where, because of larger tissue samples, most congeners were above detection, an adjusted TEQ (Adj-TEQ) was introduced utilizing only those 8 congeners that were consistently measured in most samples. The Adj-TEQ is based on 8 prominent congeners and it ignores the other congeners, resulting in somewhat lower values than the I-TEQ. I-TEQs and Adj-TEQs were highly correlated (Tables 6a and 6b).

Comparisons of the 1988 California data[40] to our study's controls revealed statistically significant decreases in the concentrations of Adj-TEQ, I-TEQ in all but one of the individual congeners examined. This first documented decrease in California body burdens[41]) is consistent with world-wide observed decreases[39]. It is believed that body burden decreases reflect lower PCDD/PCDF emissions due to implementation of pollution controls and industrial process substitutions. The one exception was 23478 PeCDF, whose levels were significantly higher in our controls. It is not clear why 23478PeCDF levels appear to have risen over the last decade.

Analyses for PCBs and OCPs are being finalized and will be available in the near future. Preliminary data from a subset of women (cases and controls combined) are compared to data from a group of 17 controls from a Canadian Breast Cancer Study [13]. Fig.4 shows the major OCPs ranked in decreasing order in our study. Not all OCPs measured in our study were measured in the Canadian study. Overall, levels appear similar, with our study showing higher levels of trans-nonachlor and oxychlordane, both metabolites of chlordane. This may reflect lower historic use of chlordane in Canada, consistent with a colder climate.

Major PCB congeners are shown in decreasing order in Fig.5 with the same Canadian population[13] used for comparison. Our data appear elevated for some congeners and similar for the rest. The overall ranking of PCBs is consistent between the two populations, with PCBs 153, 180 and 138 dominating. A number of PCB congeners were not measured in the Canadian study.

CORRELATION MATRIX

Tables 6a and 6b show the Spearman rank correlation coefficients for the major PCDD/PCDF congeners, I-TEQ, Adj-TEQ and age for cases and controls. There was a very high correlation between I-TEQ and Adj-TEQ in both the cases and the controls, confirming the validity of using the Adj-TEQ. As expected, [34] there was a positive correlation between age and most PCDD/PCDFs examined. With a few notable exceptions, the overall pattern of the correlation matrices was very similar for cases and controls. Most notably, the correlations for PeCDD were strikingly different between the two groups. Among cases PeCDD was positively correlated with all the other PCDD/PCDF congeners. Among controls, however, other than the summary measures (I-TEQ,Adj-TEQ), PeCDD was only correlated with TCDD. Also worth noting is a lack of correlation between all the furan (PCDF) congeners and age among cases and a strong positive correlation with age among the controls. These differences likely reflect differences in exposure profiles although they may also reflect differences in metabolism. A revised correlation matrix will be constructed to explore associations among all chemicals (PCDD/PCDFs, PCBs and OCPs) and age in cases and controls separately.

CASE–CONTROL ANALYSIS

Table 4 shows the summary statistics for major PCDD/PCDF congeners in cases and controls. Figure 3 shows the same distributions in box-plot format. The distribution of all the congeners was wide (i.e., large standard deviations), skewed upward and not normally distributed. Transformations to normalize the data were not successful for all chemicals. We therefore used the Wilcoxon rank sum test to assess statistical differences in the two distributions. None of the PCDD/PCDF congeners examined, or their summary measures (I-TEQ or Adj_TEQ), differed significantly among cases and controls (p-values for Wilcoxon rank sum test shown in Figure 3).

To further examine case-control differences, we used unconditional logistic regression to adjust for age. In these models, the chemical concentrations were added as continuous variables to a model with indicators for four categories of age. A separate model was run for each PCDD/PCDF congener. These results are shown in Table 7. While age-adjustment did affect the risk estimates, all odds ratios remained close to 1.0 with confidence intervals that included 1.0.

Further case-control analyses to be conducted will include: examining the effects of outliers; adjusting for other potentially important covariates in multivariate analyses; stratifying the data by factors that other studies have suggested might be important effect modifiers (e.g., menopausal status, estrogen receptor status, breastfeeding history); re-examining these congeners in the context of the organochlorine pesticides and PCBs; and grouping the chemicals by their estrogenicity and toxicity.

FUTURE WORK

Whereas the emphasis of this Final Report was placed on the novel and unique PCDD/PCDF measurements, PCBs and OCPs were also measured and these data are currently being finalised. Correlations among all body burden measurements will be examined to identify chemicals that are highly correlated with others and could, therefore, be used as surrogates resulting in a shorter list of future target analytes and better use of resources. In addition, selected chemicals will be included in models predicting disease (logistic regression) and in models predicting body burdens (multiple linear regression).

The overall strong similarity between cases and controls in this study suggests that patients with benign breast conditions may share many of the same risk factors with breast cancer patients. We plan to conduct additional analyses to further explore the relationship between some of these known risk factors and breast cancer among participants in this study. If we continue to see a lack of an association between breast cancer and the traditional risk factors, it would suggest that we have overmatched. If such were the case,

choice of another type of surgical control would be warranted in future studies. For the current study, however, the striking similarities between cases and controls makes it unlikely that our preliminary results concerning the chemical concentrations have been confounded by other potential risk factors for breast cancer.

These data will finally be combined with data from our second study on African American women from the San Francisco Bay Area. This study, currently underway, has the same exact design and tests the same hypotheses using another 50 cases and 50 controls. It is expected that the two studies combined will enhance the statistical power to examine environmental links with breast cancer and allow analysis of subgroups (i.e., ER(+) vs. ER(-), post- vs. pre-menopausal, etc.)

PRELIMINARY CONCLUSIONS

Based on the available data, the following preliminary conclusions can be drawn:

1. Cases and controls in our study are very similar on demographics and medical and reproductive profiles, suggesting that the use of benign breast controls may have resulted in over-matching. The use of other surgical controls should be explored.
2. In our effort to frequency match cases and controls, we obtained a study population comprised mostly of women in their 40s, an age group not reflecting the age distribution of the disease.
3. Chemical analysis results need to be expressed on a lipid basis because the lipid content in the specimens is highly variable. This finding raises questions regarding the validity of certain published studies where non-lipid normalized data were used.
4. Body burdens of major organochlorine analytes appear overall similar, with a few exceptions, to data reported in other similar studies, both in terms of patterns and in terms of concentrations.
5. A small but statistically significant drop in dioxin body burdens of California women was observed between a survey conducted in 1988 and the 45 controls from our study.
6. As expected, there was a positive correlation between age and most PCDD/PCDFs examined.
7. Preliminary case-control analysis, adjusted for age, revealed no statistically different concentrations of PCDD/PCDF congeners between cases and controls, but a more extensive analysis is warranted.

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Table 1. Study Patients (Cases only) vs. all Invasive Female Breast Cancer Patients treated at Stanford in 1995.*

	Study	Stanford
Age:		
< 40	10%	9%
40 - 49	48%	20%
50 - 59	28%	29%
60+	7%	42%
Non-Hispanic White	82%	80%

* Data from the California Cancer Registry

Table 2a. Distribution of selected sociodemographic characteristics among breast cancer cases and benign breast controls with p-values for the Pearson chi-square (except where noted).

Characteristic	Cases (n=50) N (%)	Controls (n=47) N (%)	p (x^2)
Age Group:			
< 40	5 (10.0)	8 (17.0)	
40-49	24 (48.0)	27 (57.5)	
50-59	14 (28.0)	8 (17.0)	
60+	7 (14.0)	4 (8.5)	0.09*
Race/ethnicity:			
Non-Hispanic White	41 (82.0)	39 (83.0)	
Hispanic	3 (6.0)	4 (8.5)	
Black	0 (0.0)	1 (2.1)	
Asian/Pacific Islander	4 (8.0)	1 (2.1)	
Other	2 (4.0)	2 (4.3)	0.58
BMI (kg/m^2):			
≤ 22	26 (52.0)	27 (57.4)	
> 22	24 (48.0)	20 (42.6)	0.59
Birthplace:			
California	17 (34.0)	19 (40.4)	
Other U.S. State	25 (50.0)	20 (42.6)	
Foreign Born	8 (16.0)	8 (17.0)	0.75
Marital Status:			
Married/lives as married	35 (70.0)	35 (74.5)	
Widowed/separated/divorced	12 (24.0)	5 (10.6)	
Never married	3 (6.0)	7 (14.9)	0.11
Lives Alone	9 (18.0)	3 (6.4)	0.08
Family Income:			
< 50,000	10 (21.7)	9 (19.6)	
50,000 – 99,999	13 (28.3)	18 (39.1)	
100,000 +	23 (50.0)	19 (41.3)	0.69*
Education			
High School Grad or lower	6 (12.0)	2 (4.3)	
College Graduate	23 (46.0)	24 (51.0)	
Masters degree	16 (32.0)	18 (38.3)	
M.D./Ph.D.	5 (10.0)	3 (6.4)	0.47
Recruitment Site:			
Stanford, Palo Alto, CA	47 (94.0)	40 (85.1)	
Kaiser, Oakland, CA	3 (6.0)	7 (14.9)	0.19

* p-values are from the Mantel-Haenszel chi-square.

Table 2b. Reported residential proximity to potential sources of environmental contaminants among breast cancer cases and benign breast controls with p-values for the Pearson chi-square.

Site	Cases (n=50) N (%YES)	Controls (n=47) N (%YES)	p (x^2)
Major highway(at least 4 lanes)	34 (68.0)	29 (61.7)	0.52
Chemical plant	3 (6.0)	3 (6.4)	0.38
Power plant	1 (2.0)	4 (8.5)	0.22
Smelter	1 (2.0)	0 (0.0)	n/a
Pulp Mill	2 (4.0)	1 (2.1)	n/a
Foundry	0 (0.0)	0 (0.0)	n/a
Mine	1 (2.0)	1 (2.1)	n/a
Oil refinery	2 (4.0)	1 (2.1)	0.35
Landfill	4 (8.0)	5 (10.6)	0.52
Airport	6 (12.0)	9 (19.1)	0.33
Other	8 (16.0)	16 (34.0)	0.04
Major transmission power lines #	8 (16.0)	10 (21.3)	0.67

Table 2c. Reported exposure to pesticides and herbicides among breast cancer cases and benign breast controls with p-values for the Pearson chi-square.

Exposure	Period of life	Cases (n=50) N (%YES)	Controls (n=47) N (%YES)	p (x^2)
Insect repellent on skin or clothing	Childhood & adolesence	35 (70.0)	35 (74.5)	0.62
	Young adulthood (20s)	38 (76.0)	38 (80.9)	0.56
	Last 10 years	29 (58.0)	36 (76.6)	0.05
Pesticides/herbicides in home or on lawn or garden	Childhood & adolesence	35 (70.0)	33 (70.2)	0.99
	Young adulthood (20s)	33 (66.0)	38 (80.8)	0.20
	Last 10 years	40 (80.0)	41 (87.2)	0.34
In a public place when insects or plants were sprayed	Childhood & adolesence	10 (20.0)	16 (34.0)	0.13
	Young adulthood (20s)	14 (28.0)	15 (31.9)	0.29
	Last 10 years	13 (26.0)	15 (31.9)	0.81
Live or work on a farm or ranch where pesticides or herbicides were used.	Childhood & adolesence	12 (24.0)	16 (34.0)	0.30
	Young adulthood (20s)	10 (20.0)	15 (31.9)	0.18
	Last 10 years	11 (22.0)	7 (14.9)	0.37
Use flea or tick control products on pets	Childhood & adolesence	19 (38.0)	26 (55.3)	0.08
	Young adulthood (20s)	19 (38.0)	29 (61.7)	0.06
	Last 10 years	39 (78.0)	34 (72.3)	0.52

Table 2d. Reported full- time, part- time or seasonally held jobs among breast cancer cases and benign breast controls with p-values for the Pearson chi-square.

Occupation	Cases (n=50) N (%YES)	Controls (n=47) N (%YES)	p (x^2)
Farmer or farm worker	5 (10.0)	7 (14.9)	0.46
Gardener or landscaper	1 (2.0)	4 (8.5)	0.15
Horticulturist or nursery worker	0 (0.0)	0 (0.0)	NA
Roadside or right-of-way brush and weed controller	0 (0.0)	0 (0.0)	NA
Pesticide or fertilizer factory worker	0 (0.0)	0 (0.0)	NA
Professional launder or dry cleaner	2 (4.0)	1 (2.1)	0.59
Factory worker	4 (8.2)	4 (8.5)	0.95
Electrical or electronic repair worker	1 (2.0)	4 (8.5)	0.15
Radar or radio operator	1 (2.0)	2 (4.3)	0.52
Telephone or telegraph operator	3 (6.0)	9 (19.2)	0.05
Hairdresser or manicurist	3 (6.0)	1 (2.1)	0.34
Textile processor	0 (0.0)	0 (0.0)	NA
Pulp and paper worker	0 (0.0)	0 (0.0)	NA
Janitor or custodial worker	1 (2.0)	2 (4.3)	0.52
Bus or truck driver	0 (0.0)	0 (0.0)	NA

Table 2e. Reported use of certain substances and appliances among breast cancer cases and benign breast controls with p-values for the Pearson chi-square.

Characteristic	Cases (n=50) N (%YES)	Controls (n=47) N (%YES)	p (x^2)
Paints, lacquers or stains	9 (18.0)	10 (21.3)	0.68
Hair dyes or tints	27 (54.0)	21 (44.7)	0.36
Hair spray	29 (58.0)	33 (70.2)	0.21
Fabric dyes	1 (2.0)	2 (4.3)	0.52
Inks	4 (8.0)	7 (14.9)	0.29
Wood dust or saw dust	5 (10.0)	11 (23.4)	0.08
Cotton or other textile fibers or dust	6 (12.0)	6 (12.8)	0.91
Insecticides or garden sprays	21 (42.0)	25 (53.2)	0.27
Petrochemical plant emissions	1 (2.0)	1 (2.1)	0.97
Grain elevator dust	1 (2.0)	3 (6.4)	0.28
Electric blankets	29 (58.0)	24 (51.1)	0.49
Electrically heated water beds	14 (28.0)	15 (31.9)	0.67
Electric mattress pads	6 (13.0)	4 (8.9)	0.53
Electric heating pads	13 (26.0)	11 (23.4)	0.77
Heater on at night while sleeping	19 (38.0)	13 (27.7)	0.28
Light on in the room, most of the night, while sleeping	5 (10.0)	6 (12.8)	0.52
Color Video Display Terminal Monitor	23 (46.0)	29 (61.7)	0.12
Monochrome Video Display Terminal (VDT) Monitor	21 (42.0)	31 (66.0)	0.02
Liquid screen Video Display Terminal (VDT) Monitor	2 (4.0)	6 (12.8)	0.05
Electric typewriter	23 (46.0)	27 (57.5)	0.37
Photocopy machine	28 (56.0)	36 (76.6)	0.03
Overhead projector	9 (18.0)	10 (21.3)	0.68
Slide projector	11 (22.0)	9 (19.2)	0.73
Electrical power tools such as for wood work	6 (12.0)	6 (12.8)	0.91
Electric sewing machine	26 (52.0)	18 (38.3)	0.18
Portable electric heater	21 (42.0)	19 (40.4)	0.88
HAM radio	0 (0.0)	2 (4.3)	0.14
Source of ionizing radiation	1 (2.0)	1 (2.1)	0.97

Table 2f. Reported medical histories among breast cancer cases and benign breast controls with p-values for the Pearson chi-square (except where noted).

Medical Condition	Cases (n=50) N (%)	Controls (n=47) N (%)	p (x^2)
Diabetes (adult onset)	1 (2.0)	0 (0.0)	1.00
High blood pressure	5 (10.0)	6 (12.8)	0.52
Heart disease	4 (8.0)	1 (2.1)	0.19
Thyroid problems	4 (8.0	8 (17.0)	0.12
Benign ovarian tumor	5 (10.0)	7 (14.9)	0.24
Family history of breast cancer	19 (38.0)	16 (34.0)	0.69
Usual Adult BMI (kg/m2):			
< 22	26 (52.0)	27 (57.4)	
> 22	24 (48.0)	20 (42.6)	0.59
Change in Adult Weight #			
< 20 lbs.	12 (24.0)	17 (36.2)	
21 – 40 lbs.	23 (46.0)	12 (25.5)	
41 – 60 lbs.	7 (14.0)	13 (27.7)	
> 60 lbs.	8 (16.0)	5 (10.6)	0.08 *
Lost 20+ lbs. due to dieting			
Yes	21 (42.8)	18 (39.1)	
No	28 (56.2)	28 (60.9)	0.93
% Change in Adult BMI ##			
< 120%	16 (32.0)	21 (44.7)	
121 – 140%	24(48.0)	12 (25.5)	
> 140 %	10 (20.0)	14 (29.8)	0.07 *

weight change = difference between the max & the min of weight at age 20, usual adult weight, current weight, and heaviest weight. ## = largest BMI/smallest BMI * * p-values are from the Mantel-Haenszel chi-square.

Table 2g. Reported radiation exposures among breast cancer cases and benign breast controls with p-values for the Pearson chi-square (except where noted).

Medical Condition	Cases (n=50) N (%)	Controls (n=47) N (%)	p (x^2)
Ever received radiation treatment	3 (6.0)	3 (6.4)	0.58
Ever received chest/back x-rays:			
Yes	38 (76.0)	40 (85.1)	
No	11 (22.0)	6 (12.8)	
Don't know	1 (2.0)	1 (2.0)	0.33
Number of chest/back x-rays in lifetime:			
None	11 (22.9)	6 (13.6)	
1-9	25 (52.1)	25 (56.8)	
10-19	6 (12.5)	9 (20.4)	
20+	6 (12.5)	4 (9.1)	0.57*
Age group received chest/back x-rays#:			
Birth to 10 yrs.	4 (10.8)	5 (12.8)	
11 to 19 yrs.	7 (18.9)	12 (30.8)	
20 to 49 yrs.	25 (67.6)	21 (53.9)	
50 + yrs.	1 (2.7)	1 (2.6)	0.35

among those reporting chest/back x-rays. * p-value is from the Mantel-Haenszel chi-square.

Table 2h. Reported reproductive characteristics among breast cancer cases and benign breast controls with p-values for the Pearson chi-square (except where noted).

Characteristic	Cases (n=50) N (%)	Controls (n=47) N (%)	p (x^2)
Age at Menarche			
≤ 12 yrs.	24 (48.0)	28 (59.6)	
> 12 yrs.	26 (52.0)	19 (40.4)	0.25
Ever pregnant:			
Yes	40 (80.0)	40 (85.1)	
No	10 (20.0)	7 (14.9)	0.51
Parity:			
Parous	37 (74.0)	33 (70.2)	
Nulliparous	13 (26.0)	14 (29.8)	0.68
Pregnancy ended in miscarriage/abortion #:			
Yes	23 (57.5)	23(57.5)	
No	17 (42.5)	17 (42.5)	1.00
Number of live births**			
1	5 (13.5)	10 (31.2)	
2	17 (45.9)	16 (50.0)	
3	11 (29.7)	2 (6.2)	
4	4 (10.8)	4 (12.5)	0.09*
Age at first live birth **			
< 30 yrs.	28 (77.8)	23 (69.7)	
30 + yrs.	8 (22.2)	10 (30.3)	0.45
Age at last pregnancy #:			
< 30 yrs.	25 (67.6)	20 (42.9)	
30 + yrs.	12 (32.4)	15 (42.9)	0.36
Ever breastfed **			
Yes	29 (78.4)	28 (84.8)	
No	8 (21.6)	5 (15.2)	0.49
Lifetime duration of breastfeeding**			
0 months	8 (21.6)	5 (15.1)	
1-5 months	11 (29.7)	5 (15.1)	
6-11 months	8 (21.6)	9 (27.3)	
12+ months	10 (27.0)	14 (42.4)	0.11*
Years since last breastfeeding ***			
1-10 yrs.	10 (37.0)	8 (34.8)	
11-20 yrs.	9 (33.3)	9 (39.1)	
20+ yrs.	8 (29.6)	6 (26.1)	0.96*

* p-values are from the Mantel-Haenszel chi-square.
\# Among those ever pregnant
** Among parous women
*** Among ever breastfeeders

Table 2i. Reported hormonal exposures among breast cancer cases and benign breast controls with p-values for the Pearson chi-square (except where noted).

Characteristic	Cases (n=50) N (%)	Controls (n=47) N (%)	p (x^2)
Oral Contraceptive(OC) Use:			
Ever for 6+ months	36 (72.0)	36 (78.3)	
Never for 6+ months	14 (28.0)	10 (21.7)	0.46
Age start using OCs (among ever users):			
≤ 18 years	6 (17.7)	11 (42.3)	
19 - 22 years	14 (41.2)	7 (26.9)	
23+ years	14 (41.2)	8 (30.8)	0.11
Duration of OC use (among ever users):			
≤ 1 year	7 (19.4)	6 (16.7)	
2-9 years	17 (47.2)	23 (63.9)	
10+ years	12 (33.3)	7 (19.4)	0.48*
Menopausal Status:			
post-menopausal	22 (44.9)	15 (34.1)	
pre-menopausal	27 (55.1)	29 (65.9)	0.29
Age at Menopause:			
< 45 years	7 (31.8)	9 (60.0)	
45-49 years	5 (22.7)	2 (13.3)	
50+ years	10 (45.5)	4 (26.7)	0.23
Hormone Replacement Therapy (HRT):			
Yes	24 (48.0)	17 (36.2)	
No	26 (52.0)	30 (63.8)	0.24
Duration of HRT use:			
≤ 1 year	9 (37.5)	5 (33.3)	
2-4 years	6 (25.0)	3 (20.0)	
5+ years	9 (37.5)	7 (46.7)	0.65*
Ever taken DES to prevent miscarriage?			
Yes	0 (0.0)	1 (2.2)	
No	50 (100.0)	44 (97.8)	0.29
Ever taken fertility drugs?			
Yes	1 (2.0)	4 (8.5)	
No	49 (98.0)	43 (91.5)	0.20
Ever taken a morning after pill?			
Yes	1 (2.0)	0 (0.0)	
No	49 (98.0)	46 (100.0)	-----
Ever taken thyroid medication?			
Yes	5 (10.0)	6 (12.8)	
No	45 (90.0)	41 (87.2)	0.67
Ever taken cortisone?			
Yes	21 (42.0)	22 (46.8)	
No	29 (58.0)	25 (53.2)	0.49

* p-values are from the Mantel-Haenszel chi-square.

Table 2j. Reported exercise habits among breast cancer cases and benign breast controls with p-values for the Mantel-Haenszel chi-square.

Exercise Habits	Cases (n=50) N (%)	Controls (n=47) N (%)	p (x^2)
Strenuous exercise during high school:			
0 hours/year	10 (20.0)	8 (17.0)	
1-99 hours/year	13 (26.0)	15 (31.9)	
100-199 hours/year	11 (22.0)	7 (14.9)	
200+ hours/year	16 (32.0)	17 (36.2)	0.86
Strenuous exercise ages 18-22:			
0 hours/year	19 (38.0)	12 (25.5)	
1-99 hours/year	15 (30.0)	14 (29.8)	
100-199 hours/year	5 (10.0)	8 (17.0)	
200+ hours/year	11 (22.0)	13 (27.7)	0.19
Strenuous exercise last 3 years:			
0 hours/year	19 (38.8)	15 (31.9)	
1-99 hours/year	14 (28.6)	15 (31.9)	
100-199 hours/year	10(20.4)	10 (21.3)	
200+ hours/year	6 (12.2)	7 (14.9)	0.54
Moderate exercise during high school:			
0 hours/year	10 (20.0)	5 (10.6)	
1-99 hours/year	17 (34.0)	19 (40.4)	
100-199 hours/year	11 (22.0)	5 (10.6)	
200+ hours/year	12 (24.0)	18 (38.3)	0.23
Moderate exercise ages 18-22:			
0 hours/year	10 (20.4)	4 (8.5)	
1-99 hours/year	18 (36.7)	17 (36.2)	
100-199 hours/year	8 (16.3)	10 (21.3)	
200+ hours/year	13 (26.5)	16 (34.0)	0.14
Moderate exercise last 3 years:			
0 hours/year	7 (14.3)	2 (4.3)	
1-99 hours/year	6 (12.2)	7 (14.9)	
100-199 hours/year	10 (20.4)	15 (31.9)	
200+ hours/year	26 (53.1)	23 (48.9)	0.51

Table 2k. Reported dietary habits among breast cancer cases and benign breast controls with p-values for the Mantel-Haenszel chi-square.

Dietary Habits	Cases (n=50) N (%)	Controls (n=47) N (%)	p (x^2)
Smoking Status			
Current	3 (6.4)	6 (12.8)	
Not Current	44 (93.6)	41 (87.2)	0.30
Alcohol Consumption (drinks/week)			
None	11 (23.4)	13 (27.7)	
0.1 – 1.5	15 (31.9)	11 (23.4)	
1.6 – 3.5	11 (23.4)	9 (19.2)	
≥ 3.6	10 (21.3)	14 (29.7)	0.72
Calorie Consumption (Kcal/day)			
≤ 1215.6	15 (31.9)	16 (34.0)	
1215.7 – 1598.0	15 (31.9)	17 (36.2)	
≥ 1598.1	17 (36.2)	14 (29.8)	0.61
Percent Calories from Fat			
≤ 28.0	16 (34.0)	15 (31.9)	
28.1 – 35.5	18 (38.3)	14 (29.8)	
≥ 35.6	13 (27.7)	18 (38.3)	0.45
Dairy Product Consumption (servings/week) (Milk, yogurt, cheese)			
≤ 9.8	11 (23.4)	20 (42.5)	
9.9 – 19.6	21 (44.7)	10 (21.3)	
≥ 19.7	15 (31.9)	17 (36.2)	0.38
Fruit and Vegetable Consumption (servings/week)			
≤ 18.9	16 (34.0)	15 (32.0)	
19.0 – 30.1	16 (34.0)	16 (34.0)	
≥ 30.2	15 (32.0)	16 (34.0)	0.80
Meat Consumption (servings/week) (Meat, poultry, fish)			
≤ 3.5	12 (25.5)	15 (31.9)	
3.6 – 6.3	18 (38.3)	17 (36.2)	
≥ 6.4	17 (36.2)	15 (31.9)	0.52
Egg Consumption (servings/week)			
None	19 (40.4)	19 (40.4)	
1	21 (44.7)	19 (40.4)	
≥ 2	7 (14.9)	9 (19.2)	0.78

Note: Subjects with daily calorie consumption < 600 Kcal. were excluded from this analysis (n=3).

Table 3. Summary of findings in similar studies. Analytes found to have a significant association with development of breast cancer are shown along with the tissue sampled and the type of lipid adjustment, if any.

TISSUE	LIPID ADJUSTMENT	ANALYTE	REFERENCE
ADIPOSE	GRAVIMETRIC	-	UNGER, 84
	GRAVIMETRIC	β-HCH	MUSSALO-RAUHAMA, 92
	GRAVIMETRIC	DDE, PCB	FALK, 92
	NONE	DDE, PCB	DEWAILLY, 94
	GRAVIMETRIC	OCDD	HARDELL, 96
	NONE	-	VAN'T VEER, 97
SERUM	NONE	DDE	WOLF, 93
	NONE		KRIEGER, 94
	GRAVIMETRIC	-	LOPEZ-CARILLO, 97
	CHOLESTEROL+TRIGLYCERIDES	PCB	MOYSICH, 98
PLASMA	NONE	HCB	DEWAILLY, 94
	CHOLESTEROL	-	HUNTER, 97

Table 4. Distributions of major PCDD/PCDF congeners (pg/g fat) among cases and controls.

	CASES							CONTROLS						
Chemical	n	% Detect	Mean	SD	Median	Min	Max	n	% Detect	Mean	SD	Median	Min	Max
OCDD	49	100	567.6	509.2	413.0	136.0	3293.0	45	100	528.3	484.6	395.8	169.0	3233.8
HpCDD	49	100	79.2	59.0	61.3	12.6	293.0	45	100	68.6	39.7	59.9	23.0	198.0
123678HxCDD	49	100	57.9	39.0	48.0	6.5	232.0	45	100	57.6	29.3	54.0	20.6	179.0
PeCDD	48	69	7.7	7.1	6.7	0.3	28.7	40	44	6.3	6.3	3.9	0.4	23.9
TCDD	45	65	4.0	3.4	3.1	0.2	13.8	43	56	3.9	3.6	3.0	0.4	19.6
23478PeCDF	49	100	10.4	6.0	9.0	3.1	26.0	45	93	10.5	5.6	8.7	2.0	26.4
123478HxCDF	43	88	5.4	3.6	4.5	1.7	22.0	43	82	5.9	7.0	4.2	0.4	47.8
123678HxCDF	44	86	4.5	2.5	4.0	0.9	14.6	43	76	4.1	2.5	3.5	0.4	13.0
I-TEQ	49	100	23.1	15.1	17.4	7.3	80.0	45	100	22.3	12.0	19.3	10.1	59.6
Adj-TEQ	49	100	20.4	14.0	15.4	3.2	72.3	44	96	19.8	10.1	17.1	8.5	50.6

Table 5. Concentrations of OCPs and PCBs (ng/g fat) among all study participants with complete data.

Chemical		n	% Detected	Mean	Std. Dev.	Median	Min.	Max.
Fat (%)		97	100	72	20	79	10	95
OCPs (ng/g fat):								
	DDE	60	100	745	364	682	120	2200
	trans-nonachlor	60	98	136	148	87	20	690
	Oxychlordane	59	97	72	57	56	17	340
	DDT	56	92	50	43	40	8	260
	HCB	61	100	46	28	35	14	170
	β-HCH	57	93	42	37	33	1	210
	Dieldrin	59	98	34	30	28	8	230
PCBs (ng/g fat):								
	153/132	72	100	152	82	131	44	549
	180	72	100	121	62	112	33	373
	74	72	100	65	42	53	20	293
	138	72	100	47	25	42	15	129
	182/187	72	100	45	24	39	14	148
	170	72	100	40	22	34	11	117
	196/203	72	100	37	28	29	6	183
	194	72	100	35	16	32	12	99
	199	72	100	32	27	25	4	160
	156	72	100	29	15	27	9	87
	118	72	100	29	17	24	6	86
	206	72	100	20	17	15	4	117
	183	72	100	17	9	15	6	73
	99/113	72	100	17	13	13	4	89

Table 6a. Spearman rank correlation matrix for dioxins, furans, and age at diagnosis among benign breast controls (n = 47).

	Adj-TEQ	I-TEQ	OCDD	HpCDD	123678-HxCDD	PeCDD	TCDD	23478-PeCDF	123478-HxCDF	123678-HxCDF
Age	0.30*	0.32*	0.13	0.00	0.38*	0.15	0.08	0.42*	0.43*	0.42*
Adj-TEQ	1.00	0.97*	0.60*	0.46*	0.81*	0.52*	0.71*	0.75*	0.68*	0.67*
I-TEQ		1.00	0.62*	0.52*	0.81*	0.45*	0.66*	0.75*	0.73*	0.75*
OCDD			1.00	0.76*	0.77*	-0.05	0.29	0.54*	0.37*	0.45*
HpCDD				1.00	0.57*	-0.15	0.29	0.41*	0.39*	0.43*
123678-HxCDD					1.00	0.14	0.35*	0.64*	0.61*	0.64*
PeCDD						1.00	0.60*	0.09	0.12	0.19
TCDD							1.00	0.46*	0.51*	0.52*
23478-PeCDF								1.00	0.68*	0.54*
123478-HxCDF									1.00	0.85*
123678-HxCDF										1.00

* p-value < 0.05

Table 6b. Spearman rank correlation matrix for dioxins, furans, and age at diagnosis among cases of invasive breast cancer (n = 50).

	Adj-TEQ	I-TEQ	OCDD	HpCDD	123678-HxCDD	PeCDD	TCDD	23478-PeCDF	123478-HxCDF	123678-HxCDF
Age	0.32*	0.25	0.04	0.13	0.28*	0.33*	0.32*	0.18	0.09	0.10
Adj-TEQ	1.00	0.95*	0.59*	0.63*	0.73*	0.84*	0.82*	0.83*	0.73*	0.75*
I-TEQ		1.00	0.64*	0.70*	0.76*	0.83*	0.82*	0.87*	0.79*	0.79*
OCDD			1.00	0.83*	0.51*	0.48*	0.45*	0.56*	0.60*	0.65*
HpCDD				1.00	0.50*	0.51*	0.47*	0.64*	0.68*	0.75*
123678-HxCDD					1.00	0.55*	0.50*	0.71*	0.62*	0.65*
PeCDD						1.00	0.74*	0.61*	0.55*	0.50*
TCDD							1.00	0.67*	0.60*	0.48*
23478-PeCDF								1.00	0.77*	0.84*
123478-HxCDF									1.00	0.89*
123678-HxCDF										1.00

* p-value < 0.05

Table 7. Crude and adjusted odds ratios (OR) with 95% confidence intervals for the interquartile range of each chemical estimated using logistic regression.

Chemical	Interquartile Range (pg/g fat)	Crude			Age Adjusted*		
		Regression Coeff (β)	Odds Ratio	95% CI	Regression Coeff (β)	Odds Ratio	95% CI
Adj-TEQ	10.23	0.0041	1.04	0.70,1.39	-0.0013	0.99	0.62,1.35
I-TEQ	11.45	0.0041	1.05	0.70,1.39	-0.0003	1.00	0.64,1.36
OCDD	318.00	0.0002	1.05	0.79,1.32	0.0002	1.07	0.80,1.34
HpCDD	48.45	0.0043	1.23	0.82,1.64	0.0042	1.23	0.81,1.65
123678-HxCDD	32.00	0.0002	1.01	0.63,1.39	-0.0011	0.97	0.57,1.36
PeCDD	8.15	0.0315	1.29	0.77,1.82	0.0255	1.23	0.68,1.78
TCDD	3.40	0.0085	1.03	0.62,1.44	-0.0064	0.98	0.55,1.41
23478-PeCDF	7.90	-0.0009	0.99	0.44,1.55	-0.0145	0.89	0.30,1.49
123478-HxCDF	3.50	-0.0148	0.95	0.67,1.23	-0.0296	0.90	0.61,1.20
123678-HxCDF	2.90	0.0535	1.17	0.67,1.66	0.0370	1.11	0.60,1.63

* adjusted for 4 categories of age.

FIG. 1. LIPID CONTENT OF BREAST ADIPOSE vs. AGE
R2 = 0.12, p<0.001, N=97

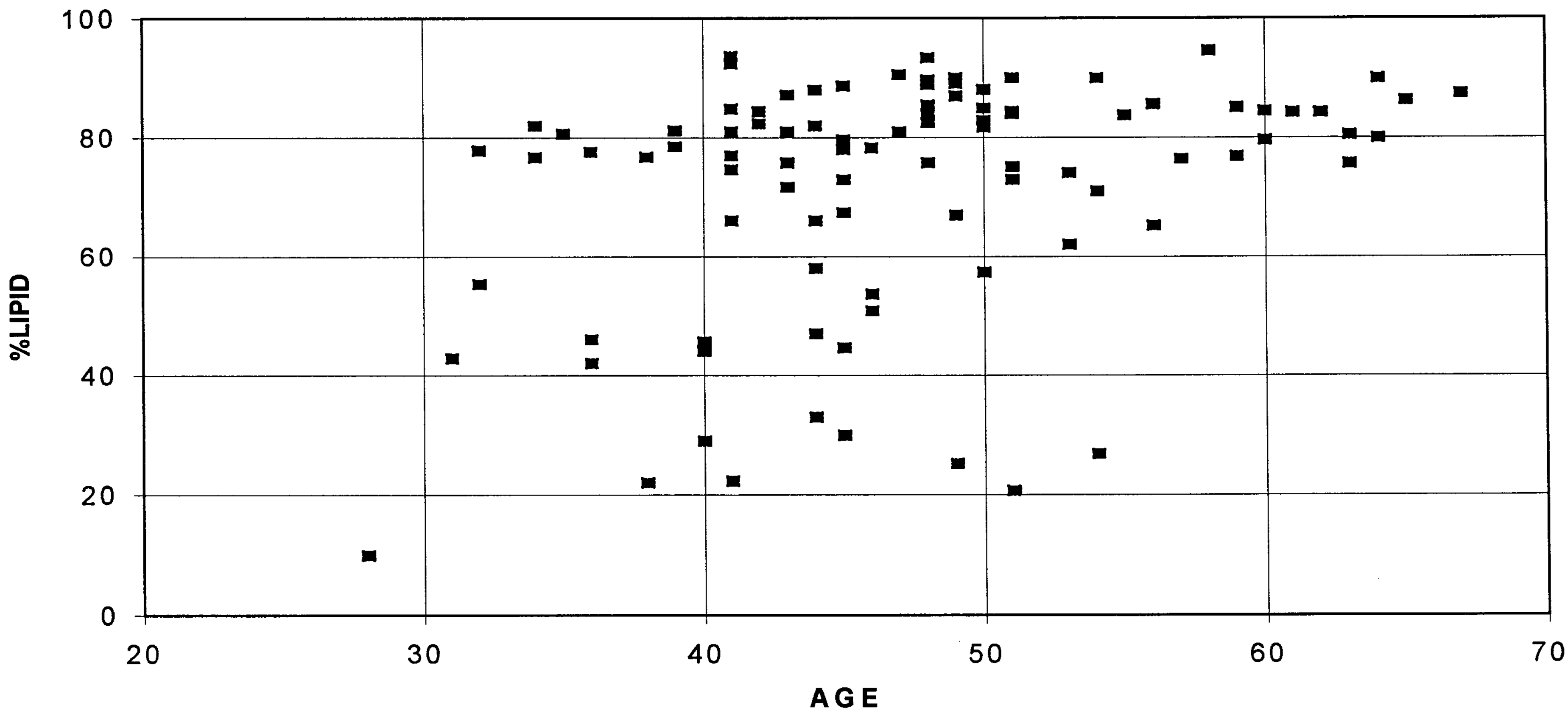


FIG. 2. MAJOR PCDD/Fs IN CASES AND CONTROLS FROM THIS STUDY
& A 1988 CALIFORNIA POPULATION

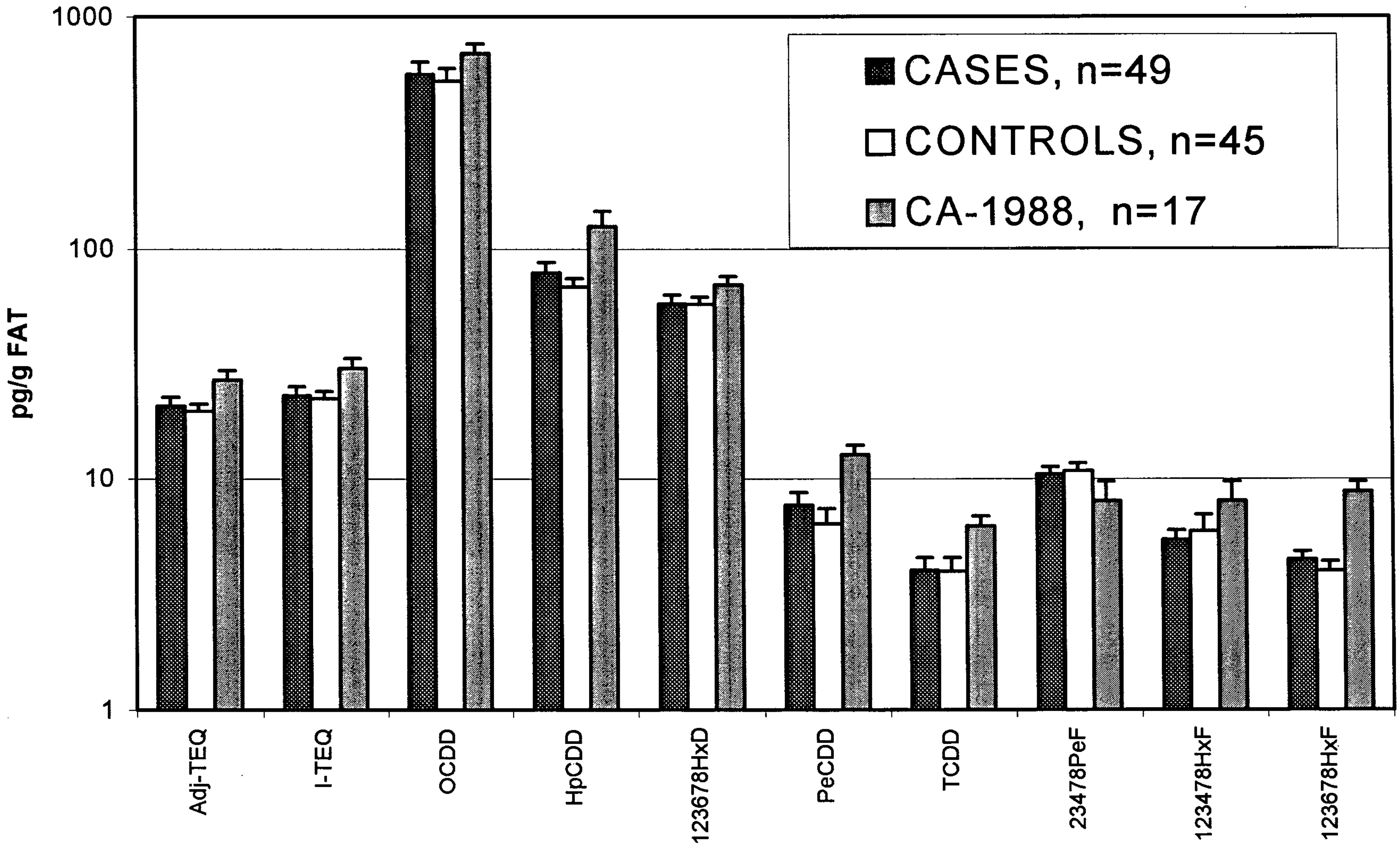


Figure 3. PCDD/PCDF distributions (pg/gram fat) for cases and controls with corresponding p-values for the Wilcoxon rank sum scores.

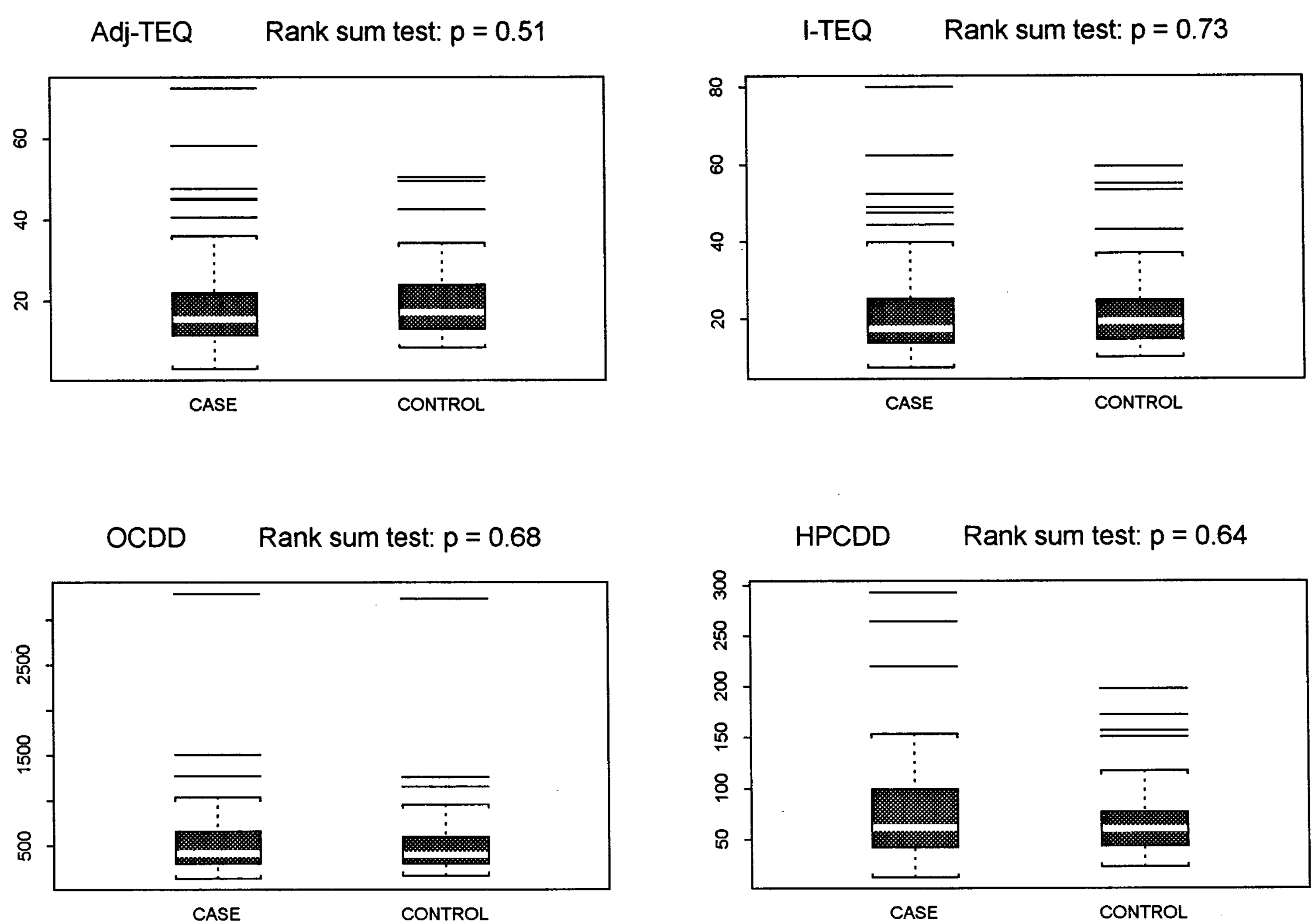


Figure 3. PCDD/PCDF distributions (pg/gram fat) for cases and controls with corresponding p-values for the Wilcoxon rank sum scores.

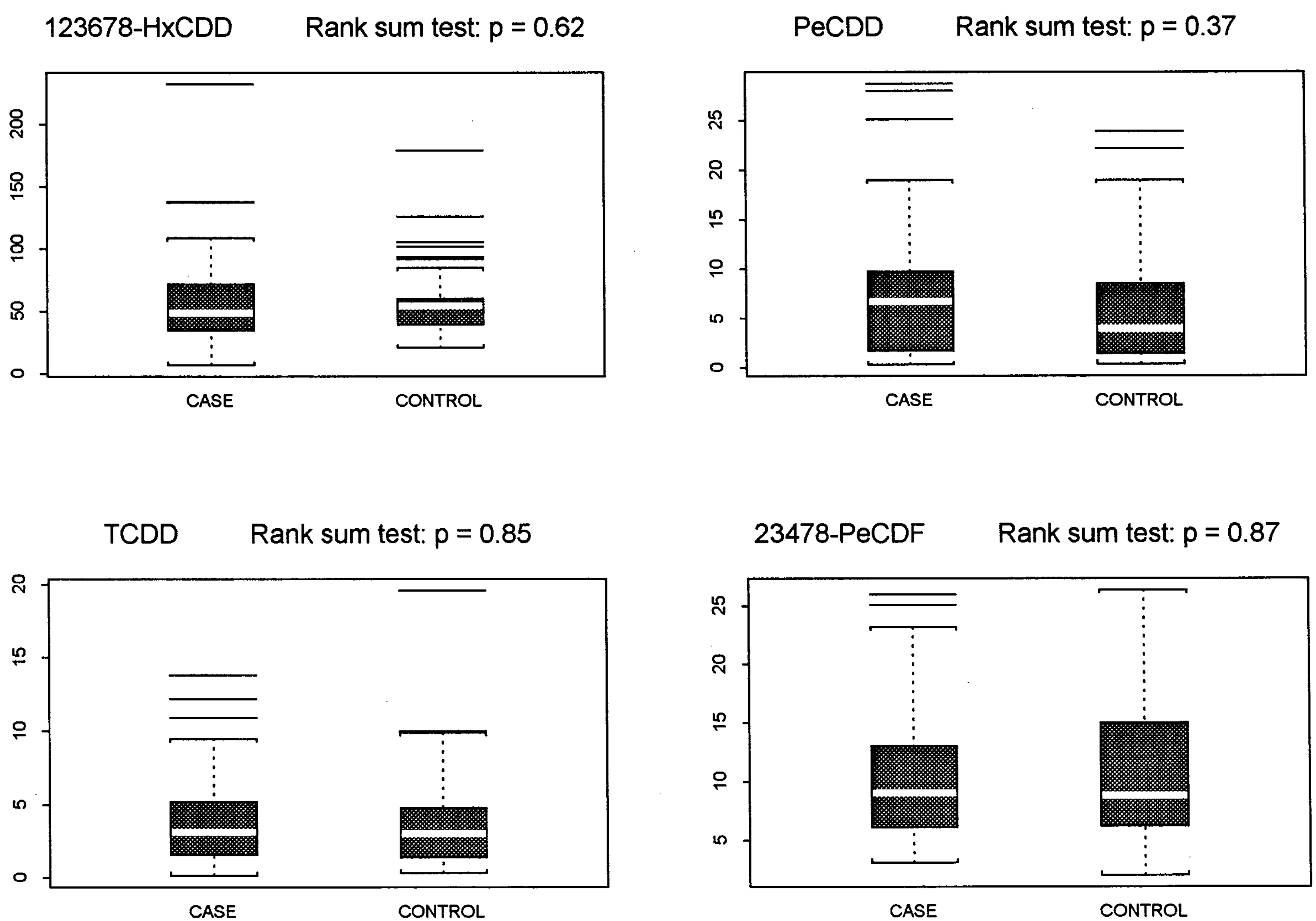
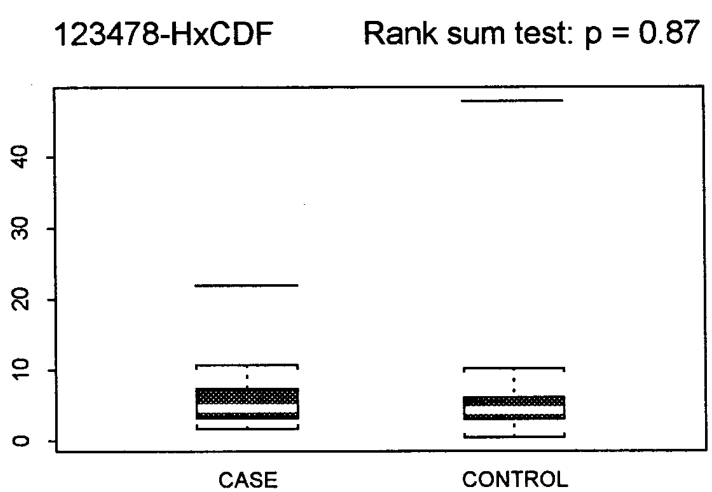


Figure 3. PCDD/PCDF distributions (pg/gram fat) for cases and controls with corresponding p-values for the Wilcoxon rank sum scores.



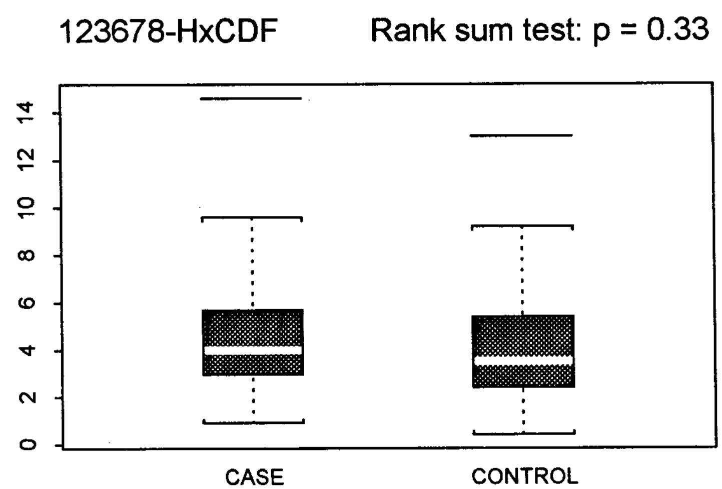


Fig. 4. MAJOR OCPs in BREAST ADIPOSE TISSUE

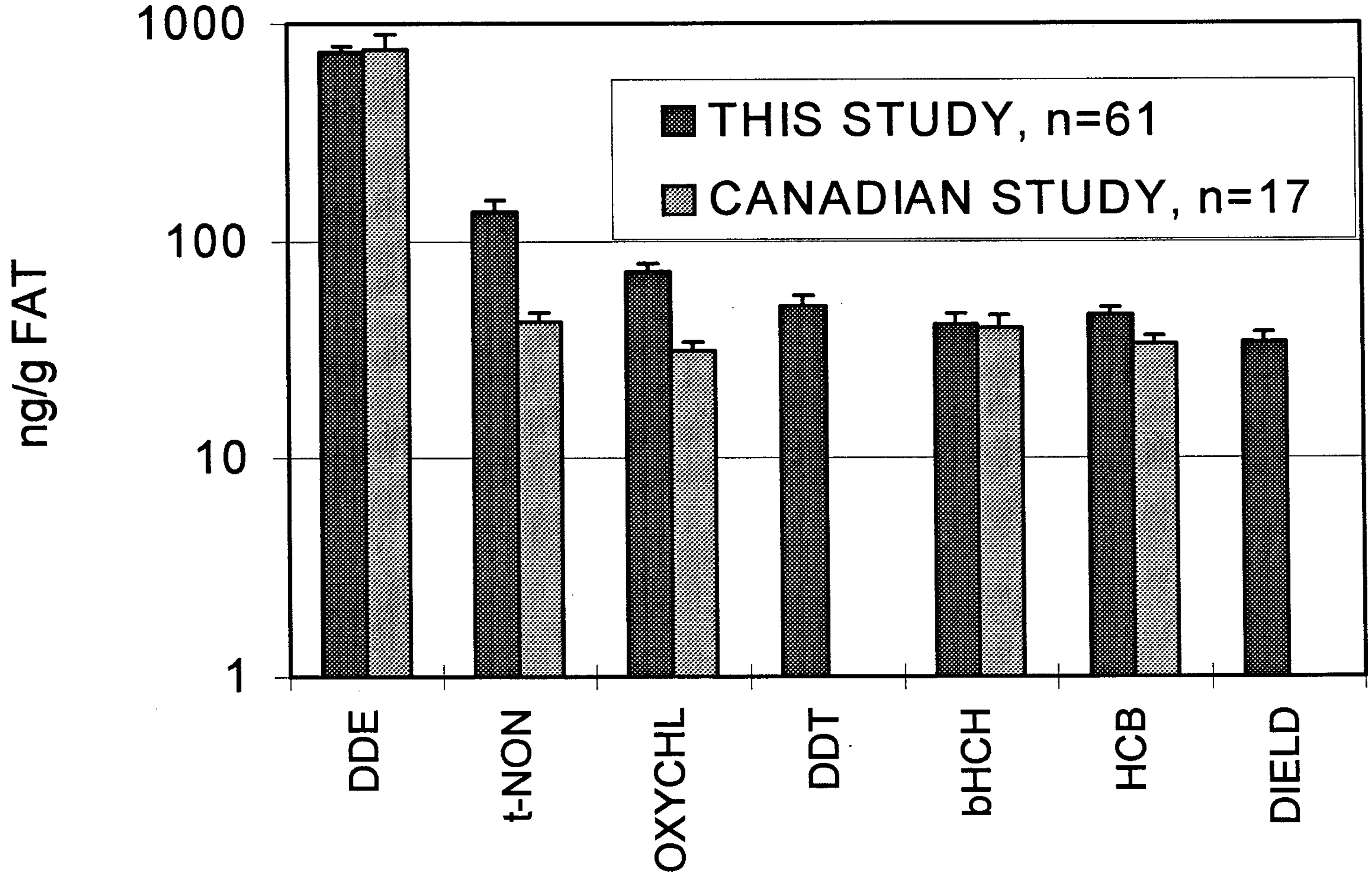
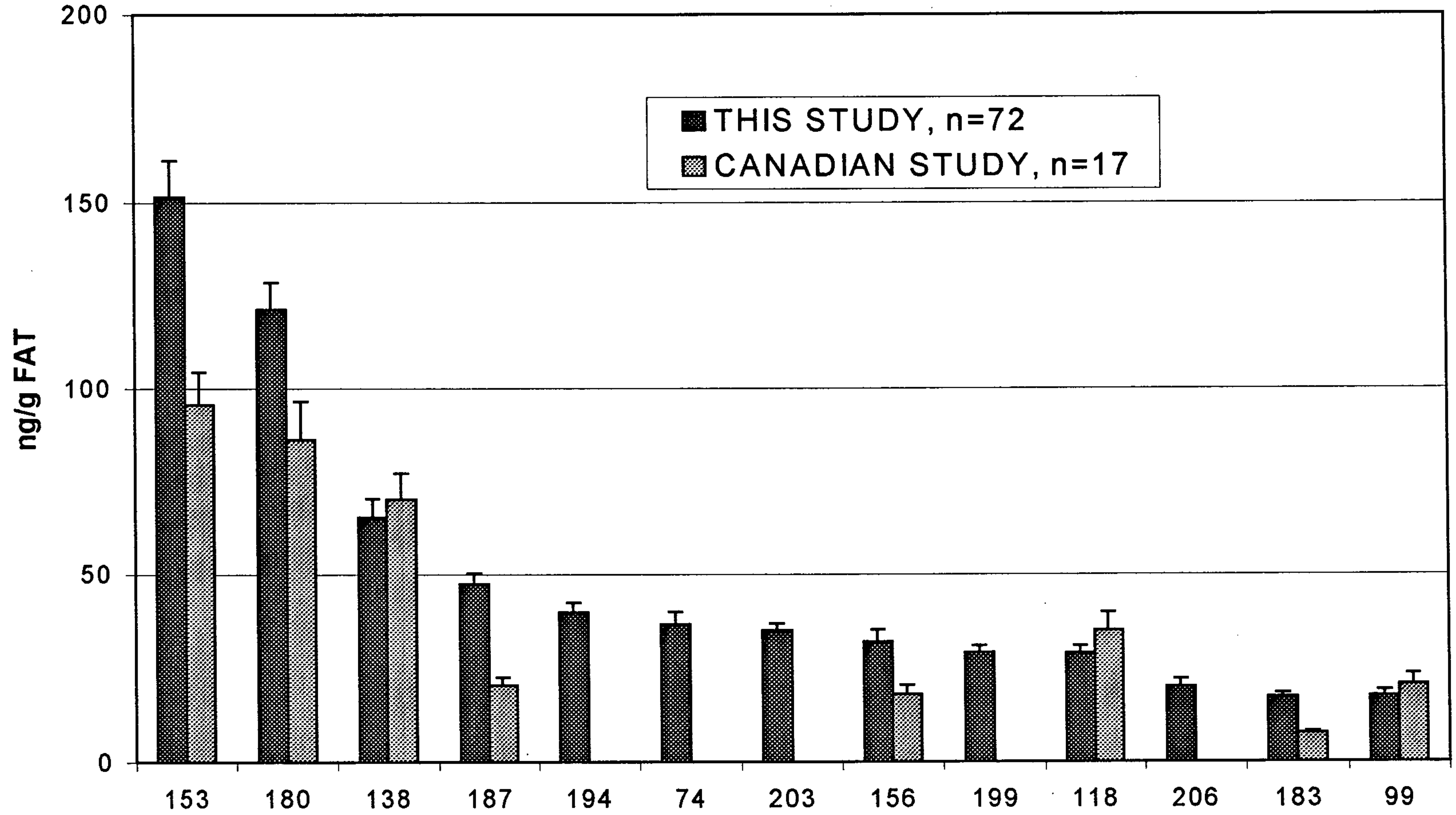


Fig. 5. Major PCB Congeners in Breast Adipose



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Publications based on this grant

1. M Petreas, J.She, J.Winkler, P.Visita, M.McKinney. Dioxins, PCBs and organochlorine pesticides in human breast adipose tissue. Proceedings of the 17th Internat Dioxin Conference, Indianapolis, 1997

2. J.She, J.Winkler, M.McKinney, P.Visita, M. Petreas. Development of an isotope dilution GC/NCI-MS method for the analysis of organochlorine pesticides in human breast adipose tissue. Proceedings of the 17th International Dioxin Conference, Indianapolis, 1997

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5. M Petreas, J She, M McKinney, P Visita, J Winkler, M Mok, K Hooper. Dioxin Body Burdens in California Populations. Proceedings of the 217th Amer Chem Soc National Meeting. Anaheim, CA, 1999